



ORIGINAL ARTICLE

Major hepatectomies for perihilar cholangiocarcinoma: Predictors for clinically relevant postoperative complications using the International Study Group of Liver Surgery definitions



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Received 22 August 2014; received in revised form 24 February 2015; accepted 1 April 2015
Available online 20 June 2015

KEYWORDS

complications;
major liver resection;
perihilar cholangiocarcinoma

Abstract *Background/aim:* Major hepatectomies are widely used in curative-intent surgery for perihilar cholangiocarcinoma, but morbidity rates are high. The aim of the study is to explore potential predictors for clinically relevant complications after major hepatectomies for perihilar cholangiocarcinoma.

Methods: Seventy patients were included. Univariate and multivariate analyses were performed for risk factors of morbidities using the International Study Group of Liver Surgery definitions.

Results: Severe morbidity rate was 36.5%. Clinically relevant posthepatectomy liver failure, bile leak, and hemorrhage rates were 24%, 22%, and 8.5%, respectively. A neutrophil-to-lymphocyte ratio > 3.3 is an independent prognostic factor for severe complications (hazard ratio = 1.258; 95% confidence interval 1.008–1.570; $p = 0.042$) while the number of blood units > 3 is an independent prognostic factor for clinically relevant liver failure (hazard ratio = 1.254; 95% confidence interval 1.082–1.452; $p = 0.003$). Biliary drainage and portal vein resection were not statistically correlated with any postoperative complication ($p \geq 0.101$). Significantly higher bilirubinemia levels were observed in patients with postoperative hemorrhage ($p = 0.023$).

Conclusion: Clinically relevant morbidity rates after major hepatectomies for perihilar cholangiocarcinoma are high. Liver failure represents the main complication and is correlated with

Conflicts of interest: None.

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<http://dx.doi.org/10.1016/j.asjsur.2015.04.007>

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the number of transfused blood units. A patient with increased bilirubinemia appears to have a high risk for postoperative hemorrhage. Biliary drainage and portal vein resection does not appear to have a detrimental effect on morbidities. Neutrophil-to-lymphocyte ratio is a novel independent predictor for severe morbidity after major hepatectomies for perihilar cholangiocarcinoma and may contribute to better and informed decision-making.

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1. Introduction

Perihilar cholangiocarcinoma (PHC) is considered as a cholangiocarcinoma involving the hilar bile duct (i.e., bile duct located between the right side of the umbilical portion of the left portal vein and the left side of the origin of the posterior portal vein).¹ Major hepatectomies with extrahepatic bile duct resection and loco-regional lymphadenectomy represent the standard approach for curative-intent surgery in the largest part of patients with PHC and have been associated with significant improvements for resectability and survival rates.^{2–6} Nowadays, decreased mortality rates after major hepatectomies were observed in referral centers,^{4–7} but for patients with PHC mortality rates are significantly higher compared with other pathologies⁸ and ranges from 1.4% to 12%.^{2–6,9,10} Major hepatectomies with zero mortality were also reported.¹¹ Conversely, morbidity rates after major hepatectomies are still high,^{8,12} particularly in patients with PHC because they are more likely to present added potential risk factors such as obstructive jaundice with or without cholangitis.^{10,12} Thus, morbidity rates after hepatectomies for PHC ranges from 43% to 81%^{2–6,9,10,13} and the main complications are represented by liver failure, hemorrhage, and septic complications due to bile leak.^{2–6,8,10,13}

In the literature, there is a broad spectrum of definitions for major liver resections.^{8,9,11,13–16} Recently, it was suggested that resection of four or more liver segments should be considered the standard definition for major hepatectomies.¹⁷ Furthermore, standard definitions and grading systems were proposed in 2011 by the International Study Group of Liver Surgery (ISGLS) for specific complications such as posthepatectomy liver failure,¹⁸ posthepatectomy hemorrhage,¹⁹ and bile leak.²⁰

Up to now, there are only several studies investigating potential risk factors for postoperative complications after liver resection for PHC and the studies do not always include patients with only major hepatectomies.^{5,6,10,11,21–25} Major hepatectomies are differently defined, and the postoperative complications are not standardized according to the ISGLS definitions or Dindo-Clavien classification,^{6,8,11,13,21–25} except in very few studies.^{5,9,10,16} Thus, there are a lack of data regarding potential predictors for clinically relevant complications after major hepatectomies for PHC and a study addressing this issue appears to be of interest.

The aim of the present study is to investigate potential risk factors for clinically relevant postoperative complications after major hepatectomies for PHC in a relatively large, single center experience, using the ISGLS definitions for specific morbidities.

2. Methods

2.1. Study population, inclusion criteria, and primary endpoint

Seventy patients, recruited from 1996 to 2012 at our Department of Surgery, were included. Inclusion criteria were as follows. (1) Final pathological diagnosis of PHC (i.e., hilar cholangiocarcinomas or intrahepatic cholangiocarcinomas invading the biliary convergence). Perihilar cholangiocarcinoma was considered according to the definition provided by Ebata et al.¹ (2) Major liver resections (defined as \geq four resected liver segments), combined with extrahepatic bile duct resection, and loco-regional lymphadenectomy. (3) Estimated future liver remnant volume \geq 30%.

The primary end point of the study was the identification of risk factors for clinically relevant postoperative complications that might be potentially useful in clinical decision-making for patients with PHC proposed for major hepatectomies.

The data of the patients were retrospectively assessed from a prospectively gathered electronic database and included pre-, intra-, and postoperative data (available for all patients). The study was approved by the Ethics Committee at our institution.

2.2. Preoperative characteristics of the patients

The median age was 59 years, with male gender predominance (40 patients, 57%). Cardiovascular comorbidities and diabetes mellitus were observed in 19 patients (27%) and five patients (7%), respectively.

Most of the patients presented with jaundice (59 patients, 84%), and 18 patients (26%) showed signs of cholangitis, due to the presence of the disease in eight patients (11%) and related to biliary drainage in 10 patients (14%).

Preoperative biliary drainage was performed for 15 patients (21%): percutaneously (5 patients, 7%), endoscopically (5 patients, 7%), or by previous surgery (5 patients, 7%). Only eight patients (11%) were considered for preoperative biliary drainage in our unit (indicated only in patients with cholangitis with impaired renal function); another five patients (7%) had already received biliary drainage while previous surgical exploration, and two patients (3%) were referred from gastroenterologists with palliation of jaundice. No patient underwent preoperative portal vein embolization.

Preoperative median serum level of bilirubin was 10.5 mg/dL, aspartate-aminotransferase 123 U/L, alanil-

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